Chronic eosinophilic pneumonia presenting with acute onset

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Summary
A 44-year-old woman was hospitalized with a 2-day history of cough, sputum, and fever. There was no history of atopic dermatitis or asthma. On admission, the chest X-ray revealed scattered infiltration in the left upper lung fields. Further examination revealed peripheral blood and bronchoalveolar lavage fluid eosinophilia. Transbronchial lung biopsy revealed eosinophilic pneumonia, with eosinophil infiltration of the alveoli, destroyed basal lumina, and connecting intraluminal fibrosis of the alveolar walls. Based on the findings, we made the diagnosis of chronic eosinophilic pneumonia. Treatment with prednisolone at 60 mg/day resulted in dramatic improvement of both the symptoms and the radiologic abnormalities. (Asian Pac J Allergy Immunol 2012;30:321-5)

Key words: chronic eosinophilic pneumonia, acute eosinophilic pneumonia, bronchoalveolar lavage fluid, steroid

Introduction
Eosinophilic pneumonia is an idiopathic disease characterized by eosinophil infiltration of the lungs. The characteristic features of chronic eosinophilic pneumonia (CEP) were originally described by Carrington and colleagues. CEP most commonly affects middle aged women. The common symptoms are cough, dyspnea, wheeze, fever, and weight loss. Typically, the onset of CEP is insidious.

CEP is associated with asthma and/or atopic dermatitis, and the symptoms of CEP have been persistent for more than a month. This condition is usually associated with alveolar and/or blood eosinophilia. The typical radiographic findings of CEP are bilateral peripheral infiltrates without hilar involvement and has sometimes been described as “radiography-negative pulmonary edema”. As demonstrated in this case, it is worth of noting that CEP can rarely present as an acute disorder in the absence of allergic triggers, and oral steroid (prednisolone: PSL) is effective.

Case Report
A 44-yr-old woman without a history of asthma or atopic dermatitis had previously presented to a clinic with cough, sputum, and fever which had begun that morning. At presentation, her chest X-ray did not show any remarkable abnormalities. Because her symptoms had not improved after 2 days, she attended our hospital. She was nonsmoker, and did not consume alcohol or use illicit drugs. She had not travelled abroad. She was living in a house with steel frame architecture, and did not have any pets or a history of exposure to any particles. The remainder of her medical, social, and family history was unremarkable.

Physical examination at presentation revealed extensive wheeze throughout the lung zones. Her temperature was 37.9°C but there were no other remarkable vital signs and physical findings. Laboratory examinations obtained at presentation revealed a total WBC count of 31,280 cells/µL with a differential of 8.0% neutrophils, 7.0% lymphocytes, 84.5% eosinophils, and 0.5% basophils. The serum level of total IgE was elevated to 528 IU/mL, serum eosinophil cationic and protein to 51.9 µg/L. Serologic tests for C-reactive protein, KL-6, and auto-antibodies including antinuclear antibody, rheumatoid factor, and P-anti-neutrophil cytoplasmic antibodies, were normal or negative. Serologic tests for parasites were negative, and stool examination revealed no ova or parasites. Arterial blood gas analysis showed pH 7.406, PaCO₂ 35.4 torr, and...
PaO\textsubscript{2} 74.9 torr. The results of pulmonary function tests (PFT) showed a reduction in the carbon monoxide diffusing capacity (DL\textsubscript{CO}) to 10.24 mL/min/torr (59.2\% of predicted), without evidence of restrictive and obstructive ventilatory defects.

The chest X-ray at presentation to our hospital showed dense bilateral consolidation of the upper lung zones, and also light patchy consolidation of the left lower lung fields (Figure 1a.). Chest computed tomography (CT) revealed non-segmental airspace consolidation with peripheral predominance. In the left upper lobe, dense consolidation with an air bronchogram was noted. Interlobular septal thickening was also noted. In the right upper lobe, centriflobular consolidation of varying density with peripheral predominance was visualized (Figure 1b.). In the lower lobes, non-segmental airspace opacities with a density varying from ground-glass to fully opaque, was seen. No pleural effusion or mediastinal lymph node enlargement was noted (Figure 1c.). A paranasal sinus CT was normal.

After admission, we performed a bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) from the left upper lobe on the day of admission. Examination of the BAL fluid revealed an increase in the number of total cells (84.8 × 10\textsuperscript{5}/mL), with a differential of 1\% neutrophils, 96\% eosinophils, 1\% lymphocytes, and 2\% macrophages. The CD4/CD8 lymphocyte ratio in the BAL fluid was 0.40. All of the microbiology studies on the BAL fluid were negative.

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**Figure 1.** Radiographic and histopathological findings
A chest X-ray obtained at the first visit to our hospital (a). Patchy consolidation is observed in the bilateral upper and left lower lung fields. A chest CT reveals non-segmental airspace consolidation with peripheral predominance. In the left upper lobe, dense consolidation with an air bronchogram and thickening of the interlobular septa is demonstrated. In the right upper lobe, centriflobular consolidation of varying density with peripheral predominance is demonstrated (b). In the lower lobes bilaterally, there are non-segmental airspace opacities, the density varying from ground-glass to completely opaque. There is no pleural effusion or mediastinal lymph node enlargement (c). Chest X-ray obtained 5 days after the initiation of steroid therapy revealed near-complete resolution of the infiltrates in her right upper lung field and improvement of the infiltrates in the left and right lower lung fields (d). Histopathologic examination of TBLB specimens reveals severe eosinophilic infiltration of the affected areas. Examination after H-E staining reveals infiltration with chronic inflammatory cells and eosinophils in the peribronchiolar region. Exudates with lymphocytic and eosinophilic infiltration are occasionally found in the alveolar septa (e, x200). EvG staining shows fibrosis in the interstitium and alveoli (f, x200). Examination after MT staining shows eosinophilic and lymphocytic infiltration with increase in the number of elastic fibers. Rupture of the elastic fibers is prominent (g, x200). Immunohistochemical staining for type IV collagen shows the destroyed basal lamina and intraluminal fibrosis connecting the alveolar walls. Deposition of collagen fibers is observed on the luminal side of the alveoli (h, x400).
Examination of the TBLB specimens revealed severe eosinophilic infiltration. On haematoxylin and eosin (H-E) staining, the specimens showed chronic inflammatory cell and eosinophilic infiltration in the peribronchial region, and occasional organization. The pulmonary interstitium and alveolar walls were swollen and expanded. The alveolar septa were occasionally filled with exudates and with lymphocytic and eosinophilic infiltration. There was no fibrinoid necrosis around the vessels. There was no evidence of eosinophilic microabscess, vasculitis, or foreign body reaction (Figure 1e.). Elastica van Gieson (EvG) staining revealed fibrosis in the interstitium and alveoli (Figure 1f.). Masson trichrome (MT) staining showed eosinophilic and lymphocytic infiltration, with an increase in the number of elastic fibers. The elastic fibers were markedly disrupted (Figure 1g.). Immunohistochemical staining for type IV collagen showed destruction of the basal lamina and intraluminal fibrosis connecting the alveolar walls. Collagen fibers were deposited in the lumen of the alveoli (Figure 1h.).

We made the diagnosis of CEP based on BAL eosinophilia and severe eosinophilic infiltration of the lung parenchyma. The patient was treated with PSL at the dose of 60 mg/day. Her chest symptoms resolved within 2 days. A chest X-ray performed 5 days after the steroid therapy revealed nearly complete resolution of the infiltrates in the right upper lung field. The other infiltrates on the left side and right lower lung fields had also improved (Figure 1d.). The infiltrates of the right upper lung field were improved on day 15 and completely resolved by day 29. The absolute eosinophil count dramatically decreased. The arterial PaO$_2$, FEV$_{1.0}$, and DL$_{CO}$ also improved gradually. The PSL dose was successfully tapered down, and she was discharged home with instructions for very slow tapering of the PSL dose (Figure 2).

**Discussion**

CEP is an idiopathic process characterized by a marked eosinophil infiltration of the lungs. CEP most commonly affects women of middle age. Although many patients are healthy without any symptoms prior to the disease onset, about a half of the patients have coexistent asthma and/or atopic dermatitis. The usual presenting symptoms are productive cough, fever, weight loss, and wheeze. Patients with acute eosinophilic pneumonia (AEP) often present within a few days of symptom onset. Patients with AEP may also complain of the aforementioned symptoms, although less frequently than patients with CEP. These symptoms are present
for more than a month in patients with CEP. CEP is insidious, and often there is a long interval between symptom onset and diagnosis. AEP frequently leads to severe respiratory failure.

The most common clinical abnormality is an elevated peripheral blood eosinophil count. Other laboratory abnormalities may include elevated serum IgE and rheumatoid factor. In AEP, however, elevation of the peripheral blood eosinophil count and serum IgE are uncommon. The most common abnormalities identified by PFT include elevated alveolar-arterial oxygen difference and decrease of the DLco. In severe cases, restrictive or obstructive ventilatory defects may also be observed. In some patients, PFT revealed a reduction of the DLco in the absence of any restrictive or obstructive ventilatory defects.

The typical radiographic pattern of CEP is bilateral peripheral parenchymal infiltrates with hilar sparing, which has been described as “radiography-negative of pulmonary edema”. On chest CT, CEP is characterized by non-segmental airspace consolidation with peripheral predominance. Pleural effusion is uncommon. Mediastinal lymph node enlargement has been described. The typical radiographic pattern of AEP is bilateral diffuse lung infiltrates. AEP is commonly associated with pleural effusion, and Kerley’s lines may be visualized on the chest X-ray, with chest CT revealing ground glass opacities (GGO) and diffuse alveolar infiltrates. The radiographic findings in this case were not typical, in that there was interlobular septal thickening with GGO and no mediastinal lymph node enlargement. In this case, the bilateral diffuse GGO and pulmonary edema in whole lung fields as seen more commonly in AEP were observed. Pleural effusion was also not observed. These findings in the patient were compatible with the diagnosis of CEP. CEP is diagnosed by the presenting symptoms, peripheral blood eosinophilia, and characteristic radiographic findings. BAL fluid also shows eosinophilia. CEP is characterized histopathologically by interstitial and alveolar infiltrates with predominantly eosinophils, lymphocytes, and histiocytes. In addition, intraluminal fibrosis and disruption of the basal lamina are also prominent. AEP is characterized histopathologically by interstitial edema and diffuse alveolar damage (DAD). In AEP, the alveolar walls are edematous and infiltrated with eosinophils and lymphocytes, with the basal lamina almost fully intact. No interstitial edema or DAD was observed in this patient. Her symptoms, radiographic and histopathological findings, besides the peripheral blood and BAL fluid eosinophilia, were compatible with CEP, although clinically, the condition presented with an acute onset. Furthermore, she did not have either a history of exposure to any particles, passive smoking, acute respiratory tract infections, drug induced pneumonia, collagen vascular diseases, nor the possibility of an unknown allergic etiology. We made the final diagnosis of CEP, not secondary but idiopathic. In CEP with an acute onset, there may be findings suggestive of AEP.

Although CEP is insidious, and there is often a long interval between symptom onset and diagnosis, a few patients of CEP present with an acute onset. CEP presenting with an acute onset is often associated with elevation of the serum IgE level as well as the patient. Treatment of CEP is based on oral corticosteroids. After initiation of treatment, the symptoms as well as the peripheral blood eosinophilia regress within a few hours and the chest radiographic findings reverse to normal within a few days. The initial dose of PSL is between 0.5 and 1 mg/kg/day. Inhaled corticosteroid therapy might also be effective. Although corticosteroid treatment always produces dramatic improvement and treatment always leads to complete resolution, relapse of CEP is observed in up to a half of the patients. Such relapse occurs most commonly while tapering the corticosteroid dose. This patient showed dramatic improvement without relapse.

In conclusion, CEP can occasionally present with an acute onset. This rare and severe disease should therefore be considered in patients presenting with an acute onset of chest infiltrates and peripheral blood eosinophilia.

References